benzhexol hydrochloride (10 mg/kg); benztropine hydrobromide (10 mg/kg); caramiphen hydrochloride (20 mg/kg), The animals were randomized to avoid identification during the observation period of one hour, which began 10 min after the injection. After (—)-hyoscyamine sulphate (20 mg/kg) a few bursts of activity were observed during the first 20 min. Twelve rats were also given saline and another twelve rats methylatropine nitrate (20 mg/kg s.c.). A high degree of activity bursts were shown in these control groups by eleven and ten rats, respectively.

In accordance with these results preliminary experiments have indicated that cholinergic drugs such as arecoline, oxotremorine, and physostigmine induce, in rats sedated by reserpine, a stereotyped behaviour characterized by locomotion, rearing, sniffing, and gnawing. Further research is in progress to give a more complete explanation for the resemblance between the proposed cholinergically-induced behaviour in reserpinized rats and the amphetamine-induced behaviour (Randrup, Munkvad & Udsen, 1963). These anticholinergic substances given to normal rats provoke the same behaviour changes (Arnfred & Randrup, 1968) as those which are completely inhibited in reserpinized rats by the same anticholinergic substances.

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The effects of (±)-amphetamine sulphate on the self-selected circadian rhythm of activity and rest in the canary

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Canaries were allowed to choose between light and darkness (Wahlström, 1964). The birds (usually males) were put singly in cages, each illuminated separately. The light is on as long as the bird does not use the night perch, one of the two perches in the cage. The recorded circadian rhythm usually consists of one period of light (activity) and one period of darkness (rest). The duration of the circadian period is counted from one waking (leaving the night perch) to the next.

(±)-Amphetamine sulphate (7.5 and 15 mg/kg) was given orally through a stomach tube as a single dose either early (AM) or late (PM) during the activity. This circadian period was counted as No. 0. The average pre-experimental duration of activity and circadian period were obtained from the five circadian periods prior to circadian period No. 0. In each experiment the differences from these averages were calculated for period No. 0 and the three following ones. The means and standard errors, given in Table 1, were calculated on corresponding differences from all experiments.

Table 1 shows two interesting features with regard to changes in activity. The expected increase in duration of activity after amphetamine was seen in the PM series, where the birds did not roost at the expected time and overslept the next morning (seen as an increase in duration of the circadian period). In the AM series, with 15 mg/kg given on an average 9.49 hr before expected roosting, there was no increase in the duration of activity. There

TABLE 1. *Changes induced by (+)-amphetamine sulphate in the self-selected circadian rhythm of the canary*

Circ. per., Duration of circadian period.

Duration of	Time of administration	Dose mg/kg	No. of experiments	Increase (mean ± standard error of mean) in hours over pre-experimental average in circadian period No. 0	1	2	3	4
Activity	AM	7·5	12	−0·13±0·25	−0·05±0·26	0·36±0·34	0·79±0·24	0·13±0·16
Activity	AM	15·0	11	−0·02±0·41	−0·79±0·33	−0·79±0·30	−0·34±0·32	−0·19±0·30
Activity	PM	7·5	12	2·60±0·93	−0·59±0·71	−0·15±0·28	−0·71±0·69	−1·22±0·72
Activity	PM	15·0	14	1·75±0·55	−0·09±0·26	−0·02±0·27	−0·34±0·25	0·23±0·31
Circ. per.	AM	7·5	12	0·06±0·07	−0·04±0·05	0·12±0·15	0·11±0·07	0·11±0·06
Circ. per.	AM	15·0	11	0·05±0·08	0·05±0·11	−0·13±0·09	−0·12±0·06	−0·17±0·13
Circ. per.	PM	7·5	12	0·41±0·16	0·05±0·14	0·20±0·12	0·05±0·14	−0·11±0·16
Circ. per.	PM	15·0	14	0·55±0·15	0·21±0·10	0·00±0·13	0·06±0·11	−0·02±0·07

was, however, a decrease in the duration of activity in the two following periods (delayed action?). The effects of amphetamine thus seem to be dependent on the timing of the drug administration and were not limited to an increased wakefulness.

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Role of catecholamines in compulsive gnawing behaviour in mice

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Apomorphine in rats induces an increased locomotor activity and compulsive gnawing, and Ernst (1967) has reported that the apomorphine-induced compulsive gnawing is not reduced by α-methyl-tyrosine. In mice even large doses of apomorphine do not induce a compulsion to gnaw. When the mice are pretreated with centrally active anticholinergics or tricyclic antidepressants, however, apomorphine also induces an intense gnaw-compulsion syndrome. Very high gnawing intensities were obtained with the tricyclic antidepressants (Pedersen, 1967).

Mice were given amitriptyline (5 or 10 mg/kg I.P.) or imipramine (20 or 40 mg/kg I.P.). Fifteen minutes later apomorphine was injected subcutaneously (10 mg/kg). The animals were placed in cages, two mice in each cage, for one hour. A cage consists of a 30 cm high box, 12×25 cm, without bottom and lid. The cages were placed on corrugated paper. If compulsion to gnaw occurred, the mice would begin to bite the paper within 5–10 min. The gnawing intensity was estimated principally as described by Ther & Schramm (1962). Five groups, each consisting of two mice, were used at each dose level.

The gnaw-compulsion syndrome was studied in mice pretreated with α-methyl-L-tyrosine (α-MT, 50 or 100 mg/kg I.P. 4 hr before test). Both doses of α-MT significantly reduced the gnawing intensities. (—)-DOPA (200 mg/kg I.P. 1 hr before testing) completely reactivated the mice pretreated with α-MT. Furthermore it was shown that pretreatment with sodium diethyldithiocarbamate (three doses of 500 mg/kg I.P., 18, 6 and 3 hr before testing) hardly affected the gnawing intensities, although the animals were markedly sedated.

The results indicate that catecholamines, probably dopamine, in mice play an important part in the mechanism, by which the gnaw-compulsion syndrome is produced by apomorphine in combination with tricyclic antidepressants.